Case Reports

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Vitritis and retinal vasculitis caused by pseudorabies virus

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Abstract

Pseudorabies virus (PRV) is a herpesvirus of swine. PRV is also called suid herpesvirus 1 and is a member of the Alphaherpesvirinae subfamily within the family Herpesviridae. The number of PRV cases worldwide is small, but in susceptible individuals, infection with this virus has a poor prognosis. Therefore, it is urgent to improve our understanding of this disease in clinical practice to avoid misdiagnosis and to identify optimal treatments. We report a patient with PRV infection who was admitted to hospital with viral encephalitis and subsequently developed intraocular infection. Because to the lack of relevant clinical experience in the treatment of this disease, we carried out experimental treatment with good therapeutic effect. This case provides a basis for clinical diagnosis and treatment of patients with PRV.

Keywords

Pseudorabies virus, vitritis, retinal vasculitis, encephalitis, rare disease, intraocular infection

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Introduction

Pseudorabies virus (PRV) is a herpesvirus of swine. The virus is also called suid herpesvirus 1, and is a member of the Alphaherpesvirinae subfamily within the family Herpesviridae.[1] PRV can cause Aujeszky's disease,[2] mainly in suidae.[3] Regions of important glycoproteins (gB, gC, gD, and gE) have been identified that may be associated with PRV adaptation to new hosts, including humans and other mammals.[4] PRV can spread

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transneuronally via direct neuron-to-neuron transmission in its natural host.[5] The infection may lead to sporadic viral encephalitis or endophthalmitis.

Previously, several cases of PRV ocular lesions have been reported.[6] The clinical signs included retinal necrosis/retinitis,[6,7] occlusive retinal vasculitis,[8,9] optic neuritis, vitritis,[7–9] and retinal detachment.[6,7] Despite active systemic antiviral therapy with/without ocular surgeries,[6–8] the prognosis of these cases was generally poor. For instance, in the study by Ai et al.,[8]final visual acuity was 0.2 in the left eye and there was slight light perception in the right eye. Here, we report a case of encephalitis with vitritis and retinal vasculitis caused by PRV who received both systemic and intravitreal antiviral therapy and ultimately achieved a relatively good prognosis.

Case report

The reporting of this study conformed to CARE guidelines.[10] All patient details were de-identified. The patient provided written informed consent for treatment and publication of this case report. The requirement for ethics review board approval was waived because of the nature of this study (case report).

A male patient in his early 40s was admitted to the Department of Neurology, Huaihe hospital, Henan University on 7 December 2020 because of intermittent high fever for 3 days. He was involved in livestock breeding and had a history of contact with domestic pigs. Three days prior to admission, the patient experienced intermittent fever up to 40.5°C accompanied by slow speech, drowsiness, slow reactions, dizziness, and blurred vision. He had received antiviral and antibiotic therapy in a local hospital, but his symptoms gradually became aggravated. He was unconscious and gibberish on admission, with slow bilateral pupil light reflex (direct and indirect). Blood oxygen saturation decreased intermittently with a minimum of 80%. On 12 December, lumbar puncture indicated intracranial pressure as high as 200 mmH_2O. Next-generation sequencing (NGS) showed 68 unique PRV sequence reads in the cerebrospinal fluid, confirming a diagnosis of PRV encephalitis. After systemic antiviral treatment, the patient's symptoms gradually improved and his vital signs remained stable. Cranial magnetic resonance imaging (MRI) showed abnormal signals in the bilateral temporal lobe, the hippocampus, and the bilateral external capsule, which were interpreted as inflammatory lesions (Figure 1). On 22 December, lumbar puncture showed normal cerebrospinal fluid pressure and NGS showed one unique PRV sequence read. The patient was able to walk with the help of family members and conduct simple conversations, but there was clear mental impairment.

On 26 December 2020, the patient was transferred to the Department of Ophthalmology because of blurred vision in the left eye. The best corrected visual acuity (BCVA) was 0.6 in the right eye and 0.1 in the left eye. Bilateral conjunctival congestion, slight aqueous flare, slow pupil light reflex, and white sheath-like retinal vessels could be observed. In the left eye, floater cells were observed in the vitreous fluid and there was mild vitreous opacity

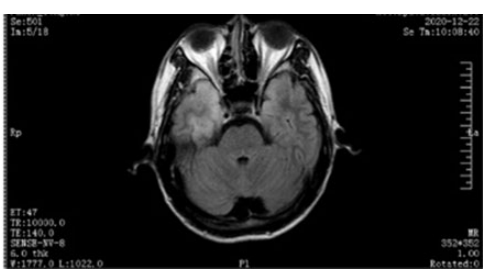

Figure 1. Cranial magnetic resonance imaging (MRI) showed abnormal signals in the bilateral temporal lobe, the hippocampus, and the bilateral external capsule.

(Figure 2a). Macular optical coherence tomography (OCT) showed a broken outer layer in the temporal macular fovea of the right eye, thinning of the macula, atrophy of the ellipsoid zone and dilated choroidal vessels in the left eye (Figure 2b). Retinal nerve fiber layer (RNFL) examination showed normal RNFL thickness in the right eye and RNFL thinning in the lower part of the left eye (Figure 3). Fundus fluorescein angiography showed that the filling time of the retinal artery and vein of the left eye was significantly delayed, with hypofluorescence corresponding to the occluded branches of retinal vessels (Figure 4).

On 1 January 2021, biopsy of vitreous fluid and intravitreal injection of 3.0 mg of ganciclovir combined with 2.4 mg of foscarnet was performed in the left eye. NGS showed 23,277 unique PRV sequence reads in the vitreous fluid. A cytometric bead array showed increased intravitreal levels of inflammatory cytokines (interleukin-6, 1247.1 pg/mL; interleukin-8, 214.7 pg/mL; and vascular cell adhesion molecule, 7598.0 pg/mL), confirming the presence of strong intraocular inflammation. Continuous systemic antiviral treatment and topical steroid eyedrops were administered. Patient consent was obtained prior to treatment.

On 29 January 2021, despite a pale optic disc (Figure 5), BCVA increased in both eyes (0.8 in the right eye and 0.3 in the left eye). The vitreous opacity in the left eye disappeared and the occlusive retinal vessels remained unchanged.

Discussion

PRV is a member of the subfamily Alphaherpesvirinae in the family

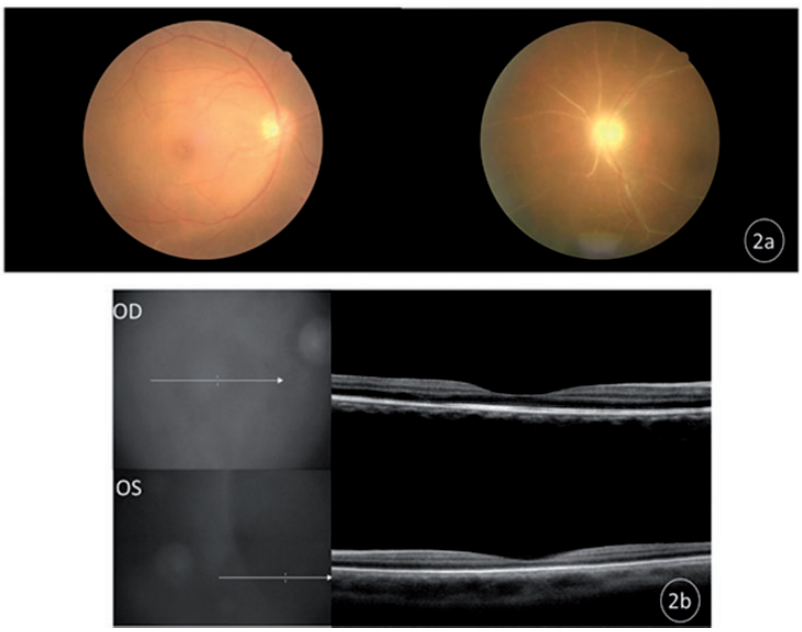

Figure 2. Bilateral white sheath-like retinal vessels and mild vitreous opacity in the left eye could be observed (a). Macular optical coherence tomography (OCT) showed a broken outer layer of the temporal macular fovea in the right eye, thinning of the macula, atrophy of the ellipsoid zone, and dilated choroidal vessels in the left eye (b).

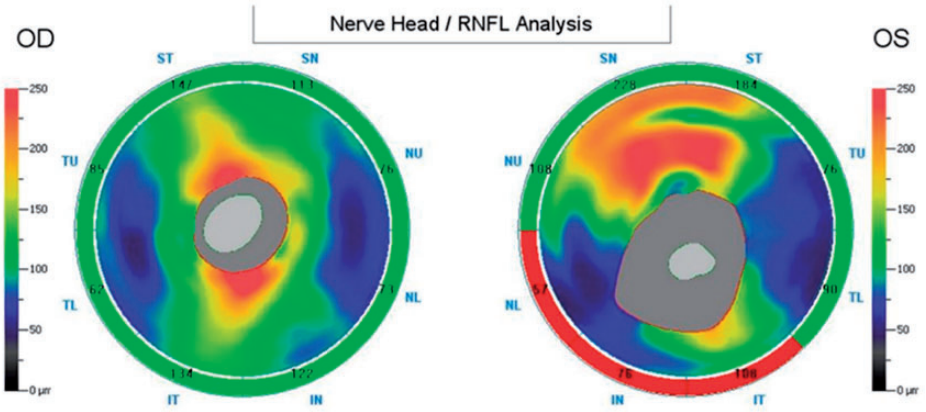

Figure 3. Retinal nerve fiber layer (RNFL) examination showed normal RNFL thickness in the right eye and RNFL thinning in the lower part of the left eye.

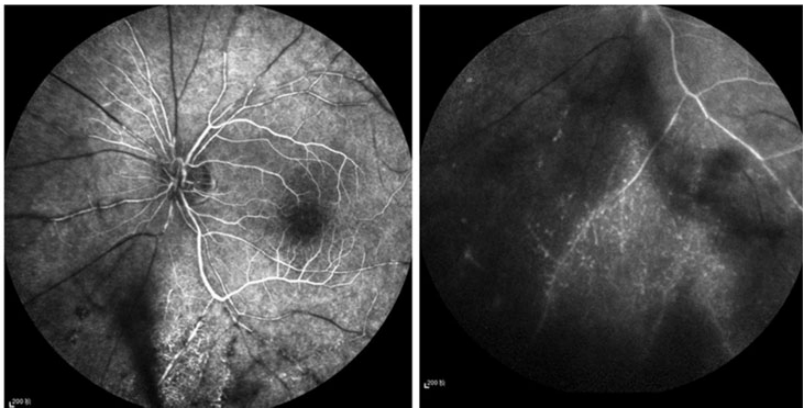

Figure 4. Fundus fluorescein angiography showed that the filling time of the retinal artery and vein of the left eye was significantly delayed, with hypofluorescence corresponding to the occluded branches of retinal vessels.

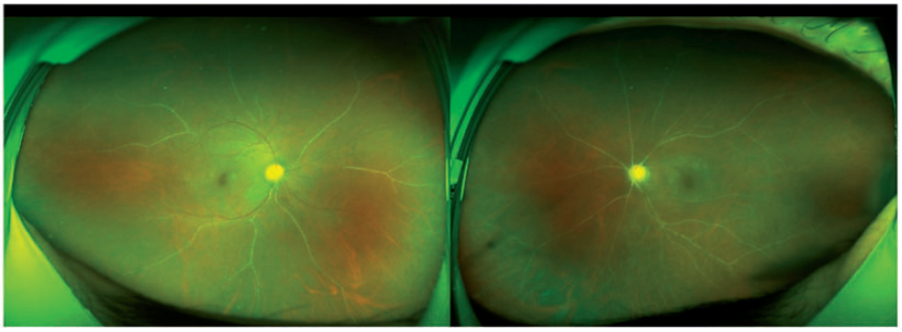

Figure 5. Bilateral pale optic disc could be observed in the patient.

Herpesviridae. Acute retinal necrosis (ARN) is caused by multiple members of this family including varicella zoster virus and herpes simplex 1 and 2.[11] The clinical signs in the present case were comparable to those of ARN and included vitreous opacity and occlusive vasculitis. Necrotizing retinitis was not observed in our patient, but was previously reported in another case with PRV endophthalmitis.[6]

Intravitreal injection of antiviral drugs such as ganciclovir and foscarnet has been widely used[12–14] for the treatment of ARN. To our knowledge, the present report is the first to use intravitreal injection of combined ganciclovir and foscarnet for the management of PRV uveitis. Four weeks after intravitreal injection, BCVA increased from 0.1 to 0.3 with improvement of vitreous opacity. Both ganciclovir and foscarnet have antiviral effects on the viral DNA polymerase; the latter is a pyrophosphate analogue that binds directly to DNA polymerase and interferes with pyrophosphate binding required for DNA polymerase activity.[15,16] In the case described here, intraocular levels of inflammatory cytokines including interleukin-8 were remarkably increased, indicating strong intraocular inflammation and providing a rationale for further anti-inflammatory therapy. Measurement of intraocular interleukin-8 levels can indicate the degree of intraocular inflammation during cytomegalovirus retinitis and may be a marker of disease recovery when assessing treatment outcome.[17–20]

According to a case series by Yang et al., patients with PRV encephalitis shared three common characteristics: occupational exposure to pig handling, acute onset with rapid progression, and clinical characteristics of central nervous system infection.[9] The clinical findings in the present case were consistent with these features.

In the current case, the progression of PRV encephalitis and endophthalmitis was inconsistent. Endophthalmitis may continue to worsen after remission of encephalitis symptoms. Because of the delayed occurrence of ocular involvement, it appears unlikely that intraocular PRV would spread transneuronally in the central nervous system instead of by hematogenous dissemination. In mammals, there are two pathways for PRV spread from the tonsils and pharyngeal epithelial cells into the cerebral cortex: either through the olfactory nerve and glossopharyngeal nerve and spinal cord, or via lymphatic vessels and lymph nodes, olfactory nerves, and the pons and spinal cord.[9,21,22] The pathway for viral spread in humans remains unclear.

Conclusion

The case described here suggests that the progression of PRV encephalitis, vitritis, and retinal vasculitis may be inconsistent: endophthalmitis may worsen after remission of encephalitis symptoms. NGS and measurement of inflammatory cytokine levels can provide evidence that permits diagnosis and assessment of intraocular inflammation. Once intraocular PRV infection has been confirmed, active systemic antiviral therapy should be administered as soon as possible. Intravitreal injections of ganciclovir and/or foscarnet may be beneficial in improving visual prognosis.

Author contributions

Conceptualization: Bo Zhao
Data curation: Manman Ying
Investigation: Manman Ying
Methodology: Manman Ying
Project administration: Xin Hu
Supervision: Xin Hu
Writing – Original Draft: Manman Ying
Writing – Review & Editing: Xin Hu

Consent and ethics statement

The patient provided written informed consent for treatment and publication of this case report.

The requirement for review board approval was waived because of the nature of this study (case report).

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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